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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,823	07/08/2005	Andreas Katopodis	TX/4-32561A	4724

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ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	

MAIL DATE	DELIVERY MODE
07/15/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,823	KATOPODIS ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *1 and 3-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *07/08/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 05/21/09 has been entered.

Claims 1-13 are pending.

2. Claims 1, 3-12 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 2 and 13 read on a method for inducing hematopoietic chimerism in a recipient of cells consisting of administering to the recipient bone marrow cells, a LFA-antibody in combination with mTOR inhibitor are under consideration in the instant application.

3. This application has been filed without formal drawing. For example, the Specification on page 14, disclosed Fig.1-3. There are no said figures in the Specification, filed on 01/31/05.

4. The specification is objected to for failing to provide a brief description of each individual Figure or Drawing disclosed on page 14 . Correction is required.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 2 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 2 is indefinite and ambiguous in the recitation of " consisting of additionally administering ...". It is unclear what Applicant means by said phrase, since the preamble of claim 2 does not recite administering of any compound, agent etc.

In view of the amendment, filed 05/21/09 the following rejections remain

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 2 and 13 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" **additionally** administering to the recipient: i) bone marrow cells or other precursor cells from the donor and ii) an anti-LFA-1 antibody in combination with...." claimed in 2 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from.

The Specification and claims only support " A method for inducing hematopoietic chimerism in a recipient of cell, tissue or organ transplant comprising administering : i) bone marrow cells or other precursor cells from the donor and ii) an anti-LFA-1 antibody in combination with... "

It is noted that Applicant does not address said rejection.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 2 and 13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 6,653,282 and newly cited US Patent' 5,284,931 , Talento et al., (Transplantation, 1993, V.55, pages 418-422), or US Patent 5,258,389 each in view of US Patent 6,486,209 and US 2002/01524900 .

Applicant's arguments, filed 05/21/09 have been fully considered, but have not been found convincing.

Applicant asserts that : the amended claims now recites administering of only an LFA-1 antibody and rapamycin. The fact that administering of only LFA-1 antibody and rapamycin would result in synergy in achieving hematopoietic chimerism was surprising and unexpected.

As initial matter, it is noted that the arguments of counsel cannot take the place of evidence in the record. In re Schulze , 145 USPQ 716, 718 (CCPA 1965). See MPEP 716.01©

Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

Regarding Applicant's statement about surprising and unexpected effects of the claimed combination. The issue is whether the properties differ to such an extent that the difference is really surprising. These effects are not surprising because co-administer of LFA-1 antibody and rapamycin together is expected to provide better efficacy than when used individually. As discussed below, at the time the invention was made each of said agents has been used to prolong graft survival and prevent rejection of organ or tissue transplants. Moreover, at the time the invention was made it was well known that additive-synergistic effects are achieved through application of each agent at relatively low dose, thereby limiting the toxicity of each individual agent while increasing the total beneficiary effect. The use of combinations therapy is so notoriously well known as to be capable of being taken by official notice. When the ingredients are associated in an obvious manner set forth in the claims, they do not co-act with each other in any new or unexpected way and define nothing patentable over the prior art. Combination therapy is used to minimize dose-dependent side effects of an individual drug.

Therefore, one of ordinary skill in the art at the time of the invention was made would expect the combination therapy of LFA-1 and rapamycin to possess the expected beneficial result that would have been produced by their combination.

US Patent '282 teaches a method of inducing immune tolerance during organ, tissue or cell transplantation including bone marrow transplantation, i.e. inducing hematopoietic chimerism, comprising administering to the subject LFA-1 antibody (see entire document, Abstract, and column 2 in particular).

Newly cited US Patent'931 and Talento et al., each teaches a method of inducing immune tolerance during organ, tissue or cell transplantation including bone marrow transplantation, i.e. inducing hematopoietic chimerism, comprising administering to the subject LFA-1 antibody.

Newly cited US Patent'389 teaches a method of inducing immune tolerance during organ, tissue or cell transplantation including bone marrow transplantation, i.e. inducing hematopoietic chimerism, comprising administering to the subject 40-O(2-hydroxyethyl)-rapamycin (see entire document, Abstract in particular).

US Patent ' 209 teaches a method of transplantation of organ, tissue or cell comprising administering to the subject an immunosuppressive inhibitor 15-deoxyspergualine (see entire document, Abstract, column 5 and claim 1 in particular).

US '490 teaches a method for inducing hematopoietic chimerism in a subject comprising administering a conventional immunosuppressant treatment using 15-deoxyspergualine (see entire document, page 4 in particular).

All the claimed elements were known in the prior art and one skill in the art could have combine the elements as claimed by known methods with no change in their respective function and the combination would have yield predictable results to one of ordinary skill in the art at the time of the invention (see *KSR International Co v Teleflex Inc*., 550U.S.-, 82 USPQ2d 1385, 2007).

Thus it would have been obvious to one of the ordinary skill in the art at the time the invention was made to combine a conventional immunosuppressant treatment with 15-deoxyspergualine with of LFA-1 antibody and 40-O(2-hydroxyethyl)-rapamycin for inducing hematopoietic chimerism with a reasonable expectation of success, because each of said agent has been used in the prior art to prevent cell, tissue and organ rejection during transplantation. "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose. . . [T]he idea of combining them flows logically from their having been individually taught in the

prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205USPQ 1069, 1072 (CCPA 1980) (see MPEP 2144.06).

Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shulka can be reached on 571/ 272-0735

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michail A Belyavskyi/
Primary Examiner, Art Unit 1644